

Herbal Drug as an Emerging Tool for Novel Drug Delivery System

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ABSTRACT

As natural sources of therapeutic agents, plant products and herbal medicines have been widely used for the treatment of various diseases due to their safety and efficacy. However, limitations such as poor solubility, low bioavailability, and instability of herbal drugs restrict their clinical application. To overcome these challenges, novel drug delivery systems (NDDS) have been introduced as promising approaches for herbal drug delivery. This review aims to summarise recent advances in herbal NDDS and highlight their role in improving therapeutic effectiveness. The literature was reviewed using databases such as PubMed, Google Scholar, and Scopus, focusing on studies related to herbal formulations incorporated into advanced delivery systems. Various nano-based systems, including liposomes, ethosomes, nanoparticles, nanoemulsions, and phytosomes, have been discussed in terms of their characteristics, advantages, and limitations. These delivery systems enhance drug stability, targeted delivery, controlled release, and bioavailability of herbal medicines. The review also emphasises current challenges and future perspectives in the development of innovative herbal drug delivery systems. Overall, herbal NDDS represent a significant advancement in improving the clinical potential of traditional medicines.

KEYWORDS: Herbal drug delivery, Novel drug delivery systems, Nano formulations, Phytomedicine Bioavailability enhancement, Liposomes, Nanoparticles

ABBREVIATIONS:

NDDS - Novel Drug Delivery System

THC – Tetrahydrocannabinol

I. INTRODUCTION

Herbal remedies have been utilised for centuries across the world, particularly in India, where traditional systems such as Ayurveda have

played a significant role in healthcare. Owing to their perceived safety, efficacy, and natural origin, herbal medicines continue to be widely used for the management of various ailments. Despite their long history of use, the clinical effectiveness of many herbal formulations remains limited due to issues such as poor solubility, low bioavailability, instability, and inconsistent therapeutic outcomes. Conventional dosage forms often fail to deliver adequate concentrations of herbal drugs at the target site, as only a small fraction of the administered dose reaches systemic circulation. In addition, the complex chemical nature of herbal constituents and variability in absorption further restrict their therapeutic potential. These limitations highlight the need for advanced approaches to enhance the delivery and performance of herbal medicines. Novel drug delivery systems (NDDS) have emerged as promising strategies to overcome the drawbacks associated with traditional herbal formulations. By improving drug stability, enhancing bioavailability, enabling targeted delivery, and providing controlled or sustained release, NDDS can significantly improve the therapeutic efficacy of herbal drugs. Nano-based delivery systems such as nanoparticles, liposomes, phytosomes, ethosomes, and nano-emulsions have gained particular attention due to their ability to enhance absorption and protect active constituents from degradation. Therefore, the integration of herbal medicines with novel drug delivery systems represents an important advancement in modern pharmaceutical research. The development of herbal NDDS not only bridges the gap between traditional medicine and modern technology but also improves the clinical potential of herbal therapies by addressing key formulation and delivery challenges.

This review aims to provide a comprehensive overview of novel drug delivery systems used for herbal medicines. The objectives of this review are to discuss the need for herbal

NDDS, summarise various nano-based delivery systems, highlight their advantages and limitations, and explore their role in improving the therapeutic efficacy and clinical potential of herbal drugs.

II. NEED FOR HERBAL NDDS

Many medications are available in a variety of forms in the contemporary pharmaceutical industry, including tablets, syrups, patches, capsules, injections, powders, gels, and more. Numerous illnesses have been treated with these traditional dose forms. In order to combat diseases as effectively as possible, both technology and human efforts have been crucial. These conventional methods, however, are today seen as antiquated and may have adverse effects, particularly in cases of chronic illness. Additionally, they may result in issues including patient non-compliance and drug resistance, particularly when intravenous therapies are involved. Synthetic medications may be harmful and lead to further health problems. However, because they are less expensive and have fewer side effects, Ayurveda and natural treatments are superior. The modern pharmaceutical industry offers a wide range of drug forms, such as tablets, syrups, patches, capsules, injections, powders, gels, and more. These conventional dosage forms have been used to treat a variety of diseases. Both human and technological efforts have been essential to fighting diseases as successfully as feasible. However, these traditional approaches are now regarded as outdated and may have negative consequences, especially when dealing with chronic illness. Furthermore, when intravenous therapies are included, they may lead to problems, including drug resistance and patient non-compliance. Synthetic drugs could be dangerous and cause more health issues. However, ayurvedic and natural remedies are better because they are less costly and have fewer side effects. All of these issues can be resolved by combining NDDS with herbal extracts. The problems with herbal medications can be fixed by encapsulating herbal extracts in nanocarriers such as liposomes, phytosomes, ethosomes, and nano-emulsions, resulting in a secure and efficient drug delivery system. This technique lowers the necessary dosage by releasing medication to the target spot at a controlled rate. Herbal NDDS is a promising strategy that can greatly aid people in light of all these benefits. Professionals from all over the world are conducting continuing research on this subject.

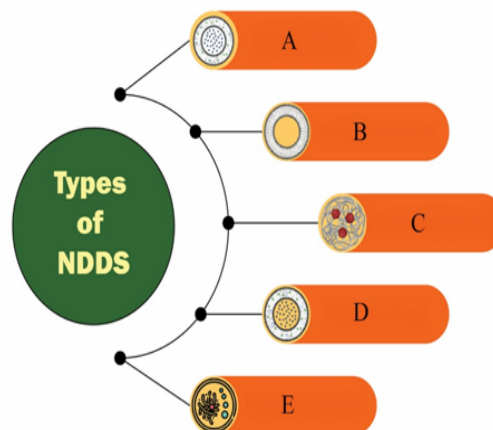


FIGURE 1.Types of herbal novel drug delivery systems (NDDS). Schematic representation showing different NDDS formulations used for herbal drugs. (A) Liposomes; (B) Phytosomes; (C) Nanoparticles; (D) Ethosomes; (E) Microspheres.

III. LIPOSOMES

They are spherical carriers that either include a portion of solvent that is freely distributed into the interior or allow the solvents to freely float inside. They are composed of polar lipids and are in diameters ranging from 0.05 to 5.0 μ m. They are made up of hydrophilic and basophilic groups.

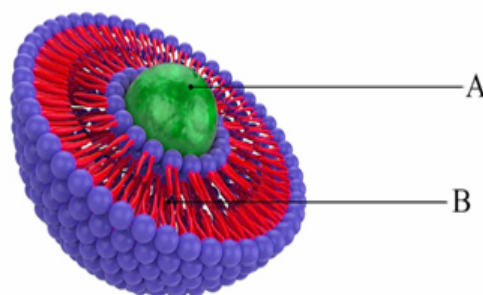


FIGURE 2.Structure of Liposome. Schematic representation showing phospholipid bilayer forming vesicles for drug encapsulation. Liposomes consist of a hydrophilic core and hydrophobic lipid bilayer suitable for both hydrophilic and lipophilic herbal actives. (A) Hydrophilic core with entrapped drug; (B) Phospholipid bilayer.

3.1 METHOD OF PREPARATION ¹³

After removing the lipids from the organic solvent and distributing them in an aqueous solution, the resulting liposomes are purified before being analysed.

3.2 ADVANTAGES

By enhancing solubility and bioavailability, these systems improve drug performance, modulate pharmacokinetics and biodistribution with enhanced intracellular uptake, and allow encapsulation of both lipophilic and hydrophilic compounds.

3.3 DISADVANTAGES

Liposomes are not economical, have restricted drug-loading capacity, are difficult and time-consuming to formulate due to the need for specialised expertise, and exhibit a short half-life.

TABLE 1: HERBAL LIPOSOMAL FORMULATION AND THEIR BIOLOGICAL ACTIVITIES ^{2,18,19}

FORMULATION	PHYTOCONSTITUENT	BIOLOGICAL ACTIVITY
Curcumin liposome	Curcumin	Anticancer
Breviscapine liposomes	Breviscapine	Cardiovascular disease
Colchicine liposome	Colchicine	Anti-gout
Liposomes encapsulated silymarin	Silymarin	Hepatoprotective

IV. PHYTOSOMES

When processed over time, several plant-based products have demonstrated a variety of biological activities and health advantages. But the majority of these are either polar or water-soluble. Their absorption is restricted as a result of these features and their enormous molecular size, which results in low bioavailability. It is frequently discovered that part or all of these compounds' action is lost after purification. This happens as a result of the components' natural interplay being disturbed. Additionally, because the stomach's acidic environment can break down extracts, they might not be safe to take orally. Phytosomes resolve these issues. They are employed to include water-soluble plant molecules or standardised plant extracts. Because they are shielded from the environment, this enhances their capacity to dissolve and be absorbed.

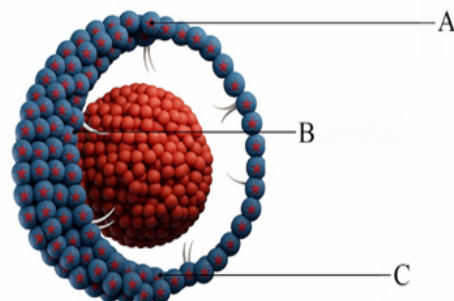


FIGURE 3. Structure of phytosomes for herbal drug delivery. Molecular complex formation between phospholipids and herbal phytoconstituents showing (A) phospholipid head with polar Phyto molecule; (B) amphiphilic Phyto phospholipid complex; (C) lipophilic tail region enhancing bioavailability.

4.1 METHOD OF PREPARATION

^{13,27}

Weigh the cholesterol and phosphatidylcholine, then dissolve them in ten millilitres of chloroform. After ten minutes of sonication, remove the organic layer to create a phospholipid layer. After hydrating with the plant methanolic extract, sonicate it once again for 20 minutes. Keep in an amber-coloured bottle.

4.2 ADVANTAGES

Phytosomes increase bioavailability, thereby reducing the required dose, and their chemical linkage with phospholipids provides improved stability.

4.3 DISADVANTAGES

Selection of an appropriate phospholipid is crucial as it affects the final product, while precise control of process parameters such as temperature, pH, and stirring speed is required to achieve phytosome formulation and prevent phytoconstituent leaching.

TABLE 2: HERBAL PHYTOSOMES AND THEIR BIOLOGICAL ACTIVITIES ^{2,18,38}

FORMULATION	PHYTOCONSTITUENT	BIOLOGICAL ACTIVITY
Ginkgo biloba phytosomes	Flavonoids	Cardioprotective antioxidant
Ginseng phytosomes	Flavonoids	Nutraceutical
Howthornphyt	Flavonoids	Cardioprot

osomes		ective & antihypertensive
Naringenin phytosomes	Naringenin	Antioxidant

V. NANOPARTICLES

Their diameters range from 10 to 1000 nanometres, making them minuscule particles. Polymeric biodegradable nanoparticles have drawn a lot of attention lately because of their advantageous properties and wide range of drug delivery applications. This method makes it possible to target medications precisely, increases their solubility, and improves the body's ability to absorb them. The active material at the centre of these nanoparticles is encased in a special polymer layer. The top-down method and the bottom-up method are the two primary approaches used in the production of nanoparticles.

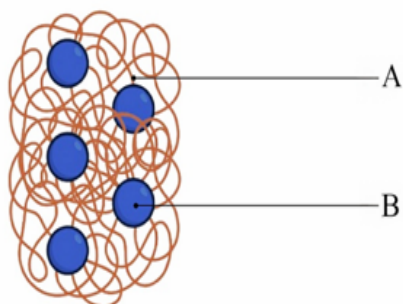


FIGURE 4. Structure of nanoparticles for herbal drug delivery. Polymeric nanoparticles showing (A) drug-loaded core containing herbal actives; (B) hydrophilic polymer coating/shell for surface modification stability.

5.1 ADVANTAGES ¹⁴

Encapsulation facilitates targeted drug delivery, enhances stability, improves pharmacokinetic behaviour and solubility, and enables efficient penetration across biological membranes.

5.2 DISADVANTAGES

Nanotechnology-based products often involve high development costs and may trigger allergic reactions when recognised as foreign particles by the body's immune system.

TABLE 3: NANOPARTICLE-BASED HERBAL FORMULATION AND THEIR BIOLOGICAL ACTIVITIES ^{1,18}

FORMULATION	PHYTOCONSTITUENT	BIOLOGICAL ACTIVITY
Artemisinin nanoparticles	Artemisinin	Anti-cancer
Glycyrrhizin acid-loaded nanoparticles	Glycyrrhizin acid	Anti-inflammatory Anti-hypertensive
Berberine nanoparticles	Berberine	Anticancer
Naringenin-loaded nanoparticles	Naringenin	Hepatoprotective

VI. ETHOSOMES

Ethosomes are said to be the ideal carrier for a transdermal delivery method, namely for drugs with limited permeability and a hydrophilic character. They work well when used topically. The higher ethanol content of ethosomes increases the drug's permeability through the skin to the deeper layer and even to the systemic circulation. An ethosome is made up of phospholipid, water, and ethanol.

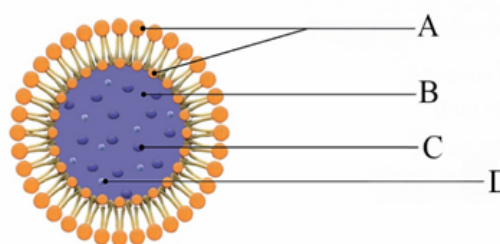


FIGURE 5. Structure of Ethosome for herbal drug delivery. (A) Hydrophilic phospholipid head groups (outer polar surface) (B) Hydrophobic phospholipid fatty acid tails forming the lipid bilayer (C) Aqueous core containing dissolved drug molecules (D) Ethanol-rich phospholipid bilayer providing membrane flexibility and enhanced skin permeability.

6.1 ADVANTAGES ¹³

Ethosomes exhibit enhanced skin permeability, demonstrate versatility in delivering lipophilic, amphiphilic, and hydrophilic drugs,

provide sustained drug release, and enable effective transdermal delivery of larger molecules.

6.2 DISADVANTAGES

Despite their advantages, these systems are associated with high production and processing costs, may occasionally cause skin irritation, and can compromise the adhesive performance of transdermal patches, limiting their suitability for all skin types.

TABLE 4: ETHOSOMES-BASED HERBAL FORMULATION AND THEIR BIOLOGICAL ACTIVITIES ^{1,18,38}

FORMULATION	PHYTOCONSTITUENT	BIOLOGICAL ACTIVITY
Cannabis sativa ethosome formulation	Tetrahydrocannabinol (THC)	Treatment of rheumatoid arthritis
Tripterygium wifordilethosome formulation	Triptolide	Anti-inflammatory

VII. MICROSPHERES

Microspheres, also referred to as micro particles, can be created using a range of synthetic and natural materials. Microspheres are made up of tiny particles with diameters ranging from 1µm to 1000µm. Both biodegradable and non-biodegradable polymers can be used to create microspheres. In recent years, microspheres and magnetic microspheres have become more prevalent. Additionally, a variety of polymers made of gelatin, albumin, and polylactic acid are available. However, the only non-biodegradable microsphere polymer approved for human use among all of these is polylactic acid. In this case, the drug release follows first-order kinetics; the matrix tubes diffuse in the first phase, after which the drug is released and dispersed within them.

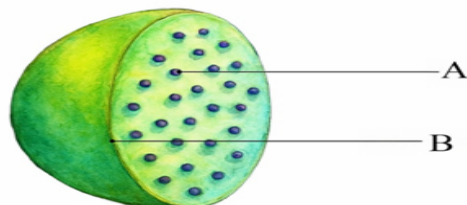


FIGURE 6. Structure of microspheres for herbal drug delivery. Polymeric microspheres showing (A)

drug-loaded polymeric matrix; (B) surface pores for sustained release of herbal actives.

7.1 TYPES OF MICROSPHERES

Based on their composition and functional characteristics, microspheres are categorised into glass microspheres, ceramic microspheres, magnetic microspheres, and radioactive microspheres.

7.2 METHOD OF PREPARATION

Microspheres can be made using techniques like polymerisation, coacervation, and hot melt extrusion.

7.3 ADVANTAGES

Microspheres enhance drug solubility and bioavailability, enable targeted and sustained drug delivery, protect sensitive drugs through encapsulation, mask the bitter taste of certain medications, and allow the use of multiple drug delivery approaches.

7.4 DISADVANTAGES

Ensuring consistent quality of the final product is challenging due to the high cost of the production process, and drug-loading capacity is limited and dependent on multiple factors.

TABLE 5: MICROSPHERE-BASED HERBAL FORMULATION AND THEIR BIOLOGICAL ACTIVITIES ^{18,10}

FORMULATION	PHYTOCONSTITUENT	BIOLOGICAL ACTIVITY
Rutin alginate chitosan microspheres	Rutin	Cardiovascular disease
Quercetin microspheres	Quercetin	Anticancer
Cynara scolymus microspheres	Cynara scolymus extract	Nutraceutical activity

VIII. TREATMENT BASED ON HERBAL NANO SYSTEM

8.1 IN TREATMENT OF LEISHMANIASIS

The infectious disease leishmaniasis is transmitted through the bite of female phlebotomine sand flies carrying the infection. This illness is more common in those who are malnourished, have compromised immune systems, or have experienced displacement. It is common in

several nations, such as Brazil, India, and some regions of East Africa. It is among the most serious infectious diseases that these areas are affected with. When the illness affects internal organs, it can be fatal in its visceral form. Pentavalent antimonial, which was widely used for many years, is part of the conventional treatment. However, their use has decreased for a number of reasons, including drug resistance, patient non-compliance, and their lack of cost-effectiveness. Although amphotericin B has been successful in treating the illness, its application is restricted due to adverse effects such as neurotoxicity and hypokalaemia. It is thought that natural substances such as alkaloids, steroids, terpenoids, curcumin, and flavonoids have antiparasitic qualities against Leishmania species. Both in vitro and in vivo investigations are now being conducted to investigate these drugs. Leishmaniasis in the Amazon region of Brazil may be treated with a nano-emulsion therapy that uses free copaiba oil. For ages, traditional folk medicine has made use of Copaiba oil. Both protozoan species showed a decrease in the number of infected macrophages in a study conducted by Morales and Cowsheds.

IX. CONCLUSION

Numerous active plant-based chemicals can be found in the vast array of plants and herbs found in Mother Nature. These substances may be helpful in the treatment of a number of illnesses. Nevertheless, a significant problem is that many of these substances are water soluble and have poor solubility and bioavailability. Because of this, these herbal remedies frequently have trouble passing through lipid-based membranes and are not efficiently absorbed into the bloodstream. The absorption rate and bioavailability of herbal extracts, including flavonoids, terpenoids, tannins, saponins, and others, greatly increase when they are standardised and mixed with nano carriers in nano drug delivery systems. Herbal medications' therapeutic effects can be improved by nano drug delivery systems, which also lessen toxicity and adverse effects. In addition to serving as nutraceuticals, this review article offers details on a variety of herbal formulations that are integrated into nano systems and have demonstrated efficacy in treating ailments like cancer, liver protection, cardiovascular illnesses, and more.

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